

REMARKS

In this Amendment, claims 57, 60-65, 69-71, 75-84 and 86 are currently amended; claims 58, 66-68 and 72-74 were previously presented; and claims 1-56, 59 and 85 are canceled without prejudice or disclaimer. Claims 87-106 are newly presented. It is submitted that no new matter has been added by virtue of the amended and new claims, which are supported by the original and prior claims and by the disclosure of the application as originally filed. Accordingly, the currently pending claims are now claims 57, 58, 60-84 and 86-106.

The amended, previously presented and new claims are presented to place the application in condition for allowance or in better form for appeal. -

Support for the Amended and New Claims

Support for one or more starting carrier substances in amended claim 57 is found in the disclosure of the instant specification on page 9, lines 23-24. Support for the language in step (b) of amended claim 57 is found in the instant specification on page 9, lines 11-13; on page 12, lines 5-6; on page 13, line 33; and on page 14, line 1 and lines 16-23. Support for amended claim 62 is found in the instant specification on page 13, line 28. Support for new claim 87 is found in the instant specification on page 10 and in claim 57. Claims that are dependent on claim 87 are supported by the instant specification and by the prior claims. Further support for claim 106 is found in the instant specification on page 11, line 28.

It is submitted that in the Remarks below, the November 30, 2004 Office Action has been considered as if it pertains to newly presented claims 87-105. Thus, this Amendment is intended to be responsive to the November 30, 2004 Office Action as if it applies to the new claims.

The claims satisfy the requirements of 35 U.S.C. §103

Claims 57-86 remain rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 5,906,830 to Farinas et al. (hereinafter "Farinas"). The Examiner characterizes Farinas as describing a carrier that is a liquid or gel or solvent that is capable of

dissolving and dispersing the active agent, which is in a supersaturated state. The Examiner further states that "the reliance on obviousness rejection over Farinas is the scientific fact that a heat step would generate the chemical reaction."

Applicants respectfully disagree that the teachings of Farinas make obvious Applicants' presently claimed invention.

It is respectfully submitted that the presently claimed invention must be considered as a whole in determining differences between the prior art and the presently claimed invention. M.P.E.P. §2141.02.

Considered in its entirety, the presently claimed invention is directed to a method containing elements that are distinct from the method disclosed and described by Farinas. In accordance with one aspect of Applicants' invention, a method of preparing a biologically active composition is provided which involves (a) supplying a composition that includes one or more carrier starting substances having a property that an included biologically active agent is either dispersed or dissolved therein up to a first degree of saturation; (b) chemically reacting the composition over a period of time to form or cleave covalent bonds and result in the formation of a liquid or solid non-crystalline carrier matrix in which (i) the biologically active agent is dispersed or dissolved up to a second degree of saturation, the second degree of saturation being greater than the first degree of saturation and (ii) precipitation of the biologically active agent is substantially inhibited after saturation of the biologically active agent in the composition; and (c) adding the biologically active agent to the composition during the period of time of chemically reacting the composition, wherein said biologically active agent is present in an amount that saturates the carrier starting substance and carrier matrix therein according to the first and second degrees of saturation.

Another aspect of Applicants' presently claimed invention is directed to a process of preparing a biologically active composition which involves (a) providing a carrier starting substance, or a mixture of two or more different carrier starting substances; (b) dissolving or dispersing a biologically active agent to a first degree of saturation in the carrier starting

substance, or the mixture thereof; (c) subjecting the carrier starting substance, or mixture thereof, to a chemical reaction over a period of time to form or cleave covalent bonds so as to form a liquid or a solid non-crystalline carrier matrix in which the biologically active agent is present at a second degree of saturation that is higher than that of step (b), so as to form the biologically active composition. In this process, the chemical reaction of step (c) can be initiated in two ways: (i) in the presence of the biologically active agent in an amount effective to obtain in the composition the second degree of saturation of the biologically active agent relative to the first degree of saturation in step (b); or (ii) in the absence of the biologically active agent, in which case the biologically active agent is added at a predetermined time after the chemical reaction is initiated, in an amount effective to obtain in the composition the second degree of saturation of the biologically active agent relative to the first degree of saturation in step (b). After this predetermined time of adding the biologically active agent, the composition is further subjected to the chemical reaction.

In contrast, the manufacturing method described by Farinas involves (a) admixing a polymeric material and a drug formulation compatible therewith to form a drug-polymer mixture; (b) calculating the depressed melting temperature of the drug-polymer admixture; (c) heating the admixture of (a) to a predetermined temperature that is effective to dissolve the drug in the polymeric material, wherein the predetermined temperature is above the depressed melting temperature calculated in step (b); and (d) cooling the heated admixture prepared in (c) to form the drug reservoir. In this method, the drug reservoir contains on the order of 0.1 wt. % to 20 wt. % drug. (Col. 3, lines 40-55 of Farinas).

A second aspect of Farinas' teaching relates to a variation of the method which involves step (a) as described above and a step (b) of heating the admixture of (a) to a predetermined temperature effective to provide a system containing two liquid phases, one of the phases comprising primarily polymeric material and a second liquid phase comprising primarily drug formulation. In step (c) the heated admixture of (b) is cooled to form the drug reservoir. In the Farinas method, the predetermined temperature is higher than the actual melting temperature of the pure drug in the drug formulation, and

the drug reservoir contains on the order of 0.1 wt. % to 20 wt. % drug. (Col. 3, lines 56-67 to Col. 4, lines 1-3 of Farinas).

Thus, it is clear that Applicants' presently claimed invention is distinct from the methods taught and described by Farinas, which do not subject the drug reservoir components to any type of chemical reaction that would involve measures resulting in the formation or cleavage of covalent bonds to produce reaction products.

It is further submitted that all claim limitations must be taught or suggested by the cited art reference. M.P.E.P. §2143.03.

Farinas does not teach, suggest or contemplate that a chemical reaction involving measures that form or cleave covalent bonds is perpetrated on the drug-polymer admixture so as to transform the admixture components into reaction products. Indeed, Farinas specifies that the contemplated invention is based on the idea that heating the components of a drug reservoir to a "carefully calculated, predetermined temperature" can result in a supersaturated system to deliver greater quantities of drug. (Col. 5, lines 50-54 of Farinas). Farinas reiterates this teaching throughout the disclosure. For example, at Col. 3, lines 1-4, Farinas discloses that the contemplated invention is a method that "involves heating the components of the drug reservoir during manufacture to a "carefully predetermined temperature" to produce a supersaturated reservoir. The carefully predetermined temperature of Farinas is for the purpose of dissolving drug (See, Col. 3, lines 47-48 of Farinas).

Thus, it is clear to the skilled practitioner that Farinas is applying just enough heat to dissolve the drug in the described system, and no more. In fact, Farinas specifically teaches away from the application of a temperature that would effect a chemical reaction leading to the formation or cleavage of covalent bonds. This is evidenced by Farinas' disclosure at Col. 6, lines 12-16, where it is stated that:

An admixture of polymer and drug is then heated to a temperature just higher than the calculated depressed melting temperature, but not so high as to result in chemical alteration or degradation of any reservoir component. (Emphasis added).

In view of the above teaching of Farinas, Applicants respectfully disagree that, in the context of Farinas, heating causes a chemical reaction to occur. It is respectfully submitted that the above teaching of Farinas belies the Examiner's reliance on Farinas as making obvious Applicants' invention due to "the scientific fact that a heat step would generate chemical reaction."

Applicants further respectfully disagree that it is a scientific fact that a heating step necessarily generates a chemical reaction. It is submitted that, in the light of the laws of thermodynamics, molecular or chemical entities exist because they typically reside in a thermodynamic state of relative stability. To alter this typical thermodynamically-stable state of a molecular or chemical entity, energy (for example, heat or another form of energy) needs to be applied to overcome the naturally stable state and transform the entity into its reaction product(s). Under certain conditions of energy input, a chemical reaction occurs and chemical bonds are formed or broken, while under other conditions, the entity remains inert to the energy input. Thus, in contrast to the Examiner's opinion, not every input of energy in the form of heat will generate a chemical reaction. It is further submitted that it is the amount and/or type of heat energy input that determines whether an entity will be shaken from its thermodynamically stable state and transformed into one or more reaction products or constituent parts. Accordingly, not all heating steps generate a chemical reaction.

Moreover, in cases where too little energy is applied, or the conditions are carried out so as to apply only a carefully predetermined amount of energy, no chemical reaction takes place. Farinas teaches this latter situation, in which just enough heat energy is applied in the disclosed method to dissolve a drug of interest, and no more. Thus, Farinas does not remotely teach that the components of the drug reservoir undergo a chemical reaction. Farinas provides a method that is distinct and different from Applicants' presently claimed invention.

On page 2 of the 11/30/2004 Office Action, the Examiner remarks that Applicants' claims "do not require that the biologically active agent remain in solution". It is submitted that Applicants' presently amended claim 57 describes that one property of the carrier matrix

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in the method is that precipitation of the biologically active agent is substantially inhibited after saturation of the biologically active agent in the composition.

In view of the clear distinctions between Applicants' presently claimed invention and the teachings and disclosure of Farinas, Applicants respectfully assert that Farinas does not make obvious the presently claimed invention, which is patentably distinguished over the teachings of Farinas. It is therefore respectfully requested that the Section 103(a) rejection be withdrawn.

Express Mail Label No.: EV 627295305 US

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CONCLUSION

Applicants respectfully submit that the application is now in condition for allowance. An action progressing this application to issue is courteously urged.

Should any additional fees be deemed to be properly assessable in this application for the timely consideration of this amendment and response, or during the pendency of this application, the Commissioner is hereby authorized to charge any such additional fee(s), or to credit any overpayment, to Deposit Account No. **50-0311**, Reference no. **28069-558 NATL**, Customer Number: **35437**.


Should an extension of time be required for the timely consideration of this Amendment and response, the Commissioner is hereby authorized to grant any such extension of time as may be necessary, and to charge any additional fee(s) owed by Applicants for such extension of time, to the above-mentioned Deposit Account, Reference and Customer Numbers.

If the Examiner believes that it would be helpful to discuss the application to advance the prosecution of the application and claims to allowance, he is respectfully requested to telephone applicants' undersigned representative at (212) 692-6742 and is assured of full cooperation in this effort.

Respectfully submitted,

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Date: March 18, 2005

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Express Mail Label No.: EV 627295305 US